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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,443	02/22/2002	Mark Ray Alvis	437252001200	6302

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,443	ALVIS ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-114* is/are pending in the application.

4a) Of the above claim(s) *11-17 and 42-114* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 18-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGEMENT OF AMENDMENT, REMARKS, IDS, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment, remarks and information disclosure statement (IDS) and Form PTO-1449 filed 03/17/05 are acknowledged, entered and considered. In view of Applicant's request claims 1, 4, 5, 7, 18-27, 30, 31 and 33-41 have been amended and claims 11-17 and 42-114 are withdrawn as non-elected invention. Claims 1-114 are now pending in the application and the Office action is directed to claims 1-10 and 18-14 as *per* elected invention.

It is noted that Applicant has elected without traverse Group I, species I (anesthetics) and subspecies A (bupivacaine) claims 1-10 and 18-14 in the communication filed 7/8/04. Claim 1 is objected because the claim is not limited to the elected species (i.e., anesthetics), rather the claim recites other members of Markush groups such as analgesics, antibiotics, sedatives, opioids and antitumor agents which were not elected. It is suggested that Applicant cancel non-elected species and limit the claim to elected species (anesthetics) because it is elected without traverse and the elected species appears to be unpatentable.

Wit respect to the IDS filed 3/17/05, the crossed over are duplicates of IDS filed 3/3/04 and are considered and initialed on the Office action of 10/20/04. In regard to Applicant's inquiry why reference No. 78 (IDS filed 5/9/02) was not initialed by the Examiner, the reference was not provided and the Examiner could not consider it. Thus, upon receipt of the reference, the Examiner will consider it.

The objections of the abstract and trademarks and the rejections under 35 U.S.C. 112, second paragraph and 35 U.S.C. 102(b) are withdrawn in view of Applicant's amendment and remarks filed 3/17/05. However, the rejection under 35 U.S.C. 103(a) over the prior art of record is maintained for the same reasons discussed in the previous Office action.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. § 103(a)

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 and 18-41 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Pavelka et al., Poster No. 137 of "Safety Following Intra-articular Injection of Neu Visc™--Two Studies" Fourth World Congress of the Oslo Arthritis Research Society International, Vienna, Austria, total pages 2, September 1999 taken with Yamahira et al (U.S. Patent No. 4,855,134), Maeda et al (Journal of Controlled Release, Vol. 62, pp. 313-324, 1999), Batyrov et al (Stomatologiya, Vol. 61, No. 2, pp. 7-10, March-April, 1982, English Abstract) and Solanki et al (Arthroscopy, Vol. 8, No. 1, pp. 44-47, 1992).

Applicant's arguments filed 03/17/05 have been fully considered but they are not persuasive. Applicant has argued that the cited prior art references must teach or suggest all of the claims limitations set forth in the pending independent claims in order to establish *prima facie* case of obviousness. The primary reference of Pavelka et al teaches the administration of no more than 3% of the lidocaine dose, which was considered clinically effective for reducing pain and thus the formulations reported by Pavelka et al could not have contained a therapeutically effective amount of lidocaine for treatment of pain or discomfort either at the time of administration or after 48 hours or more is noted. The material Pavelka used in his clinical trials was Neu Visc™, which is 65 mg/ml collagen, with 0.3% lidocaine (3 mg lidocaine per ml) added. Pavelka administered 1.0 ml of this formulation in his first study, and 2.0 ml in his second study, resulting in a lidocaine dose of either 3 or 6 mg, and as such, these low doses, lidocaine has no clinical relevance for therapeutically effective sustained relief of pain is unpersuasive. Contrary to Applicant's arguments, the primary reference of Pavelka et

al teaches the use of a formulation/composition comprising a commercially available Neu Visc™, a viscoelastic dispersion of Type I of highly purified fibrillar atelopeptide collagen containing or including 0.3% anesthetics such as lidocaine for reducing pain in osteoarthritis patients. The reference states that the purpose of the first study was to investigate the safety and effectiveness of a single intra-articular (IA) injection of Neu Visc™. The purpose of the second study was to evaluate the safety of a subsequent IA injection in the same patients. The reference concludes by stating that based on these two studies Neu Visc™ appears to be safe and effective in reducing pain in patients with osteoarthritis (OA) of the knee and suggests that a double-blind, controlled, randomized study is recommended for confirmation. Further, as acknowledged on page 21 of Applicant's remarks filed 3/17/05, the material Pavelka used is 65 mg/ml collagen with 0.3% lidocaine which overlaps with the claimed limitation of a collagen at a concentration of from about 3 mg to about 100 mg/ml and meet the limitations of claims 19 and 35 which is at a concentration of about 65 mg/ml. Thus, the reference clearly teaches use of a composition/formulation, which is safe and effective in reducing pain in patients with OA following of intra-articular injections of Neu Visc™.

Applicant asserts that the composition described by the primary reference of Pavelka et al does not meet the limitations of claim 1, and therefore, its dependent claims, and the combination of the cited secondary references do not render independent claims 1 and 27, and therefore their dependent claim obvious. A *prima* facie case of obviousness requires, *inter* alia: (1) a suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the

art, to modify the cited reference; (2) a reasonable expectation of success; and (3) that the reference teach or suggest of the elements of the claimed invention (MPEP § 2143). None of these requirements are satisfied by the cited references is unpersuasive. Contrary to Applicant's assertion, the Examiner acknowledges that the primary reference of Pavelka et al differs from claims 1-10 and 18-41 in not teaching a) the duration time of controlled release formulation, b) the ratio of collagen to pharmaceutical agent, c) the amount or the percentages of type I collagen, d) the concentration of the collagen and the pharmaceutical agent, and e) the use of anesthetics which is bupivacaine. With respect to the limitations of the duration time of controlled release formulation of at least 48 hours or at least 72 hours, these limitations are considered as functional limitations which is an expected characteristics of a composition claim, as such no probative weight is given to the claimed formulation/composition claim because the primary reference of Pavelka et al clearly teaches the use of the same composition for the same purposes of treating articular or incisional pain. However, the secondary reference of Yamahira et al teaches the use of atelocollagen which encompasses type I fibrillar collagen as a carrier for sustained-release of a medicament such as indomethane for about 3 days (72 hours) or 48 hours (See e.g., on col. 5, Experiment 1 and Experiment 2). On col. 3, lines 19-23, the '134 patent states that the ratio of the carrier and the medicament is not critical but, for example, indomethane is preferably incorporated in an amount of 0.0005 to 1 mg per 1 mg of carrier, and interferon is preferably incorporated in an amount of 10^3 to 10^8 IU per 1 mg of carrier. On line 24, the reference continues by stating that one of the characteristics of the present

invention is that the preparation can be prepared without using any specific binding agent. Thus, clearly suggesting that ratio of collagen to the pharmaceutical agent is not critical and the collagen used is non-crosslinked (i.e., no binding agent or crosslinking agent is used). On col. the reference further suggests that the preparation may be incorporated with local anesthetic agents for the intended purposes of treating joints which may includes articular surgery. Further, the reference of Maeda et al teaches the use of collagen which is type I atelopeptide collagen from the skin of bovine as a biodegradable drug carrier (See e.g., abstract, pages 314 and 323). Furthermore, the abstract of Batyrov et al clearly shows the use of collagen as carrier of local anesthetics such as trimecaine in which the collagen prolonged the effect of the local anesthetic. The reference of Solanki et al on page 46 discusses the advantages and disadvantages of using bupivacaine. The expected benefits of bupivacaine, an amide local anesthetic drug, are a popular choice for intra-articular anesthesia, postoperative pain relief, and arthroscopic surgery because of its long-half life.

The prior does not disclose the specific duration time of controlled release formulation, the ratio of collagen to pharmaceutical agent, the amount or the percentages of type I collagen and the concentration of collagen and pharmaceutical agent as claimed. However, the ranges disclosed in the prior art and claimed by Applicant overlap in scope, and as such it is conventional and within the skill of the art to optimize or select the specifics from the ranges disclosed. See *Ex parte Lee*, 31 USPQ2d 1105 (Bd. Pat. App. & inter. 1993); also, See MPEP 2131.03. Further, as acknowledged by Applicant on page 22, lines 25 to page 23, line 5, one of skill in the art

would know to adjust the amount of the composition administered, and therefore the amount of pharmaceutical agent delivered, depending on the type of surgical procedure performed, the site of the procedure and the severity or duration of pain or discomfort likely or usually associated with the procedure performed, as well as the pain tolerance of the patient and the particular composition being administered.

Thus, in view of the above, one of ordinary skill in the art would have been motivated at the time the invention was made to apply the teachings of the secondary references of Yamahira et al (i.e., the duration time of controlled release formulation and the ratio of collagen to the pharmaceutical agent); Maeda et al (use of type I atelopeptide collagen as biodegradable drug carrier); Batyrov et al (use of collagen as a carrier for prolonging the effect of local anesthetic; and Solanki et al (use of anesthetic such as bupivacaine for postoperative pain relief and arthroscopic surgery) to the primary reference of Pavelka et al which teaches the use of a formulation/composition comprising a commercially available Neu Visc™, a viscoelastic dispersion of Type I of highly purified fibrillar atelopeptide collagen containing or including 0.3% anesthetics such as lidocaine for reducing pain in osteoarthritis patients because such features of using collagen as a carrier for prolonging the effect of local anesthetic with controlled release formulation are known or suggested in the art, as seen in the secondary references, and including such features of using the sustained release preparation into the formulations/compositions of the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

Therefore, in view of the combined teachings of the prior art and in view for the reasons discussed above; one of ordinary skill in the art would have been motivated at the time the invention was made to employ or use the subject composition in combination with other materials to provide a wide variety of applications or may be tailored for specific applications in the manner claimed. Therefore, the combined teachings of the prior art makes obvious the claimed invention's composition/formulations for the treatment of post-surgical articular or incisional pain or discomfort consisting essentially of an aqueous dispersion of insoluble non-crosslinked type I fibrillar atelopeptide collagen and a pharmaceutical agent which is anesthetic such as bupivacaine or lidocaine, wherein the composition/formulation is formulated to release an effective amount of the pharmaceutical agent form the collagen for at least 48 hours or 72 hours. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the prior art teachings would have been obvious because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Betz*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

ACTION IS FINAL

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

4. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272 0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ROBERT A. WAX
PRIMARY EXAMINER
At Unit 1653

AM Mohamed/AAM
June 06, 2005